REMARKS/ARGUMENTS

The Pending Claims

Claims 1, 7-15, and 17-26 are pending. Pursuant to a restriction requirement, claims 7-14 and claims 21-26 have been withdrawn. Therefore, claims 1, 15, and 17-20 currently are subject to examination.

The Amendments to the Claims

Claim 1 has been amended to delete reference to assaying the copy number of SEQ ID NO: 1 and amplification of SEQ ID NO: 1. Claim 15 has been cancelled, and the dependencies of claims 17, 18, and 20 have been adjusted accordingly. No new matter has been added by way of these amendments.

Discussion of Claim Objection

The Office Action objects to claim 15 for allegedly failing to further limit the subject matter of claim 1 from which it depends. In order to advance prosecution of the present application, claim 15 has been cancelled, thereby rendering the objection moot.

Discussion of Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1, 15, and 17-20 are rejected under Section 112, first paragraph, as allegedly lacking enablement. The Office Action contends that claims 1 and 15-20 are not enabled for several reasons: (1) practicing the claimed invention is allegedly unpredictable because the application does not adequately describe the nature of a "control sample," (2) the specification describes detection of macaque homologs of Cripto-1, but allegedly fails to disclose detection of SEQ ID NO: 1, and (3) according to the Office, the disclosed macaque model of SHIV is not a predictable animal model of human HIV infection, and (4) gene expression in the brain is highly variable among primate species. This rejection is traversed for the reasons set forth below.

Contrary to the allegations of the Office Action, the present application combined with the knowledge in the art at the time the subject application was filed provides sufficient guidance to one of ordinary skill in the art for selecting and using an appropriate "control

sample" in the method defined by claim 1. The specification discloses that a control sample contains genomic DNA of a mammal that is known not to have a neurodegenerative disease (see specification at, e.g., paragraph 0019). This is further illustrated by Example 1 of the present application, which indicates that the controls were macaques that were not infected with SHIV. Thus, the application provides specific guidance as to an appropriate control sample to employ in the method defined by claim 1.

The Office Action alleges that the specification does not disclose any working examples illustrating the detection of SEQ ID NO: 1, which is the nucleic acid sequence encoding the human Cripto-1 protein, but instead discloses the detection of the macaque homolog to Cripto-1. However, Applicant is not required to provide working examples of the claimed invention. Indeed, such a requirement to provide a working example with respect to a human Cripto-1 homolog would be nothing short of a requirement to conduct clinical trials as a prerequisite to patentability. The law does not require this of Applicants. Furthermore, the Office has provided no reasoning to support the conclusion that the methods demonstrated in the macaque models could not also be successfully applied in a human. Methods for assaying overexpression of Cripto genes, including human Cripto-1, are disclosed in the specification(see specification at, e.g., paragraphs 0020-0029, and Example 5). Moreover, one of ordinary skill in the art would understand and be able to apply such methods to human Cripto-1 (SEQ ID NO: 1) without engaging in undue experimentation.

While the Office Action raises concerns regarding data normalization and the purported unpredictability associated with measuring and correlating altered gene expression to a particular phenotype, the examples cited by the Office Action do not provide specific evidence to question the ability to detect NeuroAIDS by assaying Cripto-1 expression levels. The Office is reminded that the applicant does not have to prove that a correlation exists between a particular activity and an asserted use of a compound as a matter of statistical certainty.

The Office Action also doubts the predictability of using SIV- or SHIV-infected macaques as models of HIV-induced neurological disease in humans. In particular, the Office Action alleges that Raghavan et al., *Brain Pathol.*, 7: 851-861 (1997) demonstrates varied responses to SHIV infection across different macaque species. This isolated example

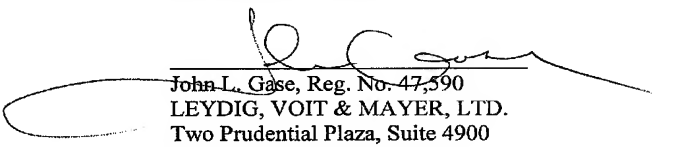
of suspected species-specific differences in the response to HIV infection in macaques does not take away from the numerous other reports of brain histopathology resulting from SIV infection in macaques, as disclosed in the application (see specification at, e.g., paragraph 0069), or from the fact that such brain histopathology was comparable to that observed in humans with NeuroAIDS (see specification at, e.g., paragraph 0069).

In view of the amendments to the claims and the foregoing arguments, the specification enables the subject matter defined by claim 1, and claims 15 and 17-20 depending therefrom. Accordingly, Applicants request withdrawal of the enablement rejection.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



John L. Gase, Reg. No. 47,590
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson Avenue
Chicago, Illinois 60601-6731
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

Date: December 12, 2008